Applicants

Gao et al.

Serial No.

09/457,066

## Appendix

On page 11, please replace the paragraph spanning lines 13-18 with the following:

[Fig. 1 is] <u>Figs. 1A-1G are</u> a Hopp/Woods hydrophilicity profile of the amino acid sequence shown in SEQ ID NO:2. The profile is based on a sliding six-residue window. Buried G, S, and T residues and exposed H, Y, and W residues were ignored. These residues are indicated in the figure by lower case letters.

Amino acid sequence changes are made in zvegf3 polypeptides so as to minimize disruption of higher order structure essential to biological activity. In general, conservative amino acid changes are preferred. Changes in amino acid residues will be made so as not to disrupt the cystine knot and "bow tie" arrangement of loops in the growth factor domain that is characteristic of the protein family. Conserved motifs will also be maintained. The effects of amino acid sequence changes can be predicted by computer modeling as disclosed above or determined by analysis of crystal structure (see, e.g., Lapthorn et al., ibid.). A hydrophobicity profile of SEQ ID NO:2 is shown in [Fig. 1] Figs. 1A-1G. Those skilled in the art will recognize that this hydrophobicity will be taken into account when designing alterations in the amino acid sequence of a zvegf3 polypeptide, so as not to disrupt the overall profile. Additional guidance in selecting amino acid substitutions is provided by the alignment of mouse and human zvegf3 sequences shown in Fig. 6.

